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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,631	04/09/2004	Kurt Vagle	PRO.12	9020
61638	7590	01/11/2007		
SIGMA-ALDRICH CO. 3050 SPRUCE STREET ST. LOUIS, MO 63013			EXAMINER KRISHNAN, GANAPATHY	
			ART UNIT	PAPER NUMBER
			1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/821,631	Applicant(s) VAGLE ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/29/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 12 has been renumbered claim 11.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the conversion of the terminal hydroxyl group of an oligonucleotide into a phosphate monoester and its deprotection, does not reasonably provide enablement for the removal of the phosphate protective groups and the base protective groups of the oligonucleotide in a single deprotection step as instantly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

- (A) The breadth of the claims
- (B) The state of the prior art
- (C) The level of predictability in the art
- (D) The amount of direction provided by the inventor
- (E) The existence of working examples
- (F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claim 1 is drawn to a method wherein the two phosphate protective groups and the base protective group of the oligonucleotide in a single deprotection step. The term phosphate protective group includes several groups having the phosphate moiety including PO_4^- and the term base protective groups is also seen as broad that includes any base protective group.

The state of the prior art

It is well known in the art of nucleotide synthesis that several protective groups are available for the protection of the base moiety and several phosphoramidites for the protection of the hydroxyls as the phosphate ester.

The level of predictability in the art

There is not seen sufficient data to substantiate the claim that the base protective groups and the phosphate protective groups can be removed in a single deprecation step. This is highly unpredictable since the base protective groups need not necessarily be

removed by using reagents and conditions that remove the phosphate protective groups.

This is dependent on the type of groups used for the protection.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the method of deprotection as instantly claimed. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for the same.

The existence of working examples

The working examples set forth in the instant specification are drawn to the preparation and deprotection of oligodeoxynucleotide 9 (pages 20 and 33 of the specification). The example doesn't show the one step deprotection of the phosphate protective groups and the base protective groups. Applicant is therefore not entitled to all that is encompassed by the instant claim.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the method as instantly claimed. One of ordinary skill in the art would have to carry out the process in order to determine if such a single step deprotection can be done using several combinations of groups. Undue experimentation is needed.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a method of converting a terminal hydroxyl group into a phosphate monoester by coupling a phosphoramidite reagent to the terminal hydroxyl group but also further recites removal of the phosphate protective groups. The overall method is not a conversion. It is not clear what applicants intend.

Claims 3 and 4 recite the notations SPOS and DMT. It is not clear what applicants intend by these notations. Notations should be followed by the expansion for the same at the first occurrence.

Claim 5 is drawn to a phosphoramidite reagent that has the substitution W, which is a nucleosidic group. According to the method of claim 1, from which claim 5 depends, a phosphoramidite reagent is coupled with the hydroxyl group of an oligonucleotide. This means that the phosphoramidite does not have a nucleoside moiety attached to it. It is not clear what applicants intend.

Claims 5 and 6 recite Z as an optional spacer group that can be alkenyl or oligoethylene glycolyl, which may be substituted. The claim does not further define the substitutions. The specification (page 16) does not define the substitutions either. In the absence of the specific moieties intended as "substitutions" or attachment to the chemical core claimed, the term "substituted" renders the claims in which it appears indefinite in all occurrences wherein

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applicant fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will facilitate substitution, requisite to identifying the composition of matter claimed.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

The closest prior art is Guzaev et al, Tetrahedron , 1995, 51, 9375-84 (document AI in IDS).

Conclusion

1. Claims 1-10 are rejected
2. Claim 11(renumbered), drawn to structural formula 2' is seen to be free of prior art.

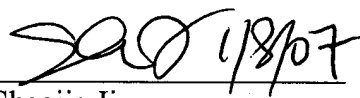
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK


Shaojia Jiang
Supervisory Patent Examiner
Art Unit 1623